Bronchiectasis: a new look at an old adversary

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Summary

The management of bronchiectasis is finally advancing and patients have new options in terms of diagnostics, antibiotic therapy and physiotherapy. The principles of management have not changed, but with some simple interventions patients can experience improved quality of life and health outcomes. Many treatments developed for cystic fibrosis are now being applied to the management of bronchiectasis due to other causes.

Key words: antibiotics, cystic fibrosis.

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Introduction

For many healthcare professionals, the term 'bronchiectasis' conjures up a bygone era of cold damp houses and coughing children. Today there is a revived interest in this condition among respiratory physicians and after many stagnant years we are able to offer something new.

The management of cystic fibrosis has rapidly improved over the past 20 years with vastly improved life expectancies. Research has flourished, and many treatments developed for the management of cystic fibrosis-related bronchiectasis are already being used in non-cystic fibrosis bronchiectasis sufferers in the clinical setting. Compared to other respiratory disorders such as asthma, evidence for the safety and efficacy of treatments used in bronchiectasis is scarce.

What do general practitioners want to know?

There are a number of commonly asked questions regarding bronchiectasis in general practice.

What monitoring is appropriate and when?

The advent of high resolution CT scans means there is a new gold standard for diagnosis.[1] We are able to assess the anatomy and severity of patients with known disease more accurately as well as diagnosing new patients. High resolution CT chest scanning should be performed at diagnosis and as determined by clinical progress. Chest X-rays are most useful in evaluating complications such as pneumonia.

Functional monitoring with spirometry (and lung volumes where available) is very useful and should be performed both during exacerbations and in stable periods. The frequency of testing will depend on the deterioration and exacerbation rate for the individual patient.

When is the best time to perform sputum cultures?

Sputum cultures should be done when the patient is stable and, ideally, not taking antibiotics. This information can then be used to guide the management of their next exacerbation. Patients on long-term macrolide antibiotics can still be managed along the same lines, as these drugs (in the low doses used) have little effect on actual pathogens isolated and on antibiotic susceptibility profiles.

If no sputum culture is available for a particular patient, collect a sample then treat for the more common pathogens, for example *Haemophilus influenzae*, with drugs such as amoxycillin/clavulanic acid or roxithromycin. If the patient fails to respond, consider treating empirically for pseudomonas pending the results of sputum culture.

Does pseudomonas colonisation matter?

We know a lot more about this pathogen than we used to. We are now aware that it forms three-dimensional structures, referred to as biofilms, which adhere to the respiratory epithelium and resist antibiotic penetration. Patients colonised with pseudomonas have a worse prognosis and more rapid decline in lung function than those who are not.[2] During an exacerbation, patients with pseudomonas should be treated aggressively with antipseudomonal antibiotics. A suitable oral antibiotic would be ciprofloxacin for at least 14 days. Patients who develop resistance to ciprofloxacin should be considered for combination treatment with ciprofloxacin and nebulised aminoglycoside (for example tobramycin). This is usually best administered in consultation with a hospital respiratory outpatient unit. Inpatients are usually treated with ticarcillin/clavulanic acid combined with an inhaled or intravenous aminoglycoside. For chronic colonisation, patients should probably have a trial of long-term macrolide antibiotics.[3]

Is physiotherapy still important and is there anything new?

Physiotherapy is still considered an essential part of bronchiectasis management and research has consistently shown it to be of benefit. For example, patients with cystic fibrosis had a faster decline in lung function when they were non-compliant with chest physiotherapy. Options for physiotherapy are broader than they used to be. Easy to use

hand-held devices such as positive expiratory pressure or flutter devices in addition to active-cycle breathing techniques are an option for many patients. Postural drainage still has a place for heavy sputum producers. Refer your patients to a local respiratory physiotherapist for advice on this important management tool.

Should my patient be on long-term antibiotics?

The cautious answer to this question is, 'We don't know'. There has been a lot of research in this area in cystic fibrosis. Several large clinical trials of macrolide antibiotics in cystic fibrosis have shown improvements in various clinical outcomes including sputum production and quality of life.[3] A lot of bench research has shown that macrolide antibiotics have anti-inflammatory effects and this may be the mechanism by which they help in cystic fibrosis. Many respiratory colleagues now give patients a trial of a low-dose regular macrolide, for example azithromycin 250 mg daily or clarithromycin 125 mg twice a day, for a few months and assess for improvements in sputum production and exacerbation rates. A large randomised controlled trial of this strategy has not yet been done.

Should my patient be on inhaled corticosteroids?

Bronchiectasis is an inflammatory condition in which the ongoing damage of the airways is due to the inflammatory response to pathogens. Inhaled corticosteroids reduce this inflammatory damage. Several randomised controlled trials have shown a benefit of inhaled corticosteroids in patients with bronchiectasis, with the main improvements being reduced sputum production and exacerbations.[4]

Are there any new medications to assist sputum clearance?

Drugs to assist sputum clearance are seeing a revival with research into using two osmotic agents – nebulised hypertonic saline and inhaled mannitol. Both of these agents have been shown to assist sputum clearance predominantly by increasing hydration of the sputum and improving the viscosity. Hypertonic saline has been shown to reduce exacerbation rates in a large cystic fibrosis trial.[5] In non-randomised studies, mannitol improved airway clearance and quality of life in patients with non-cystic fibrosis bronchiectasis. A large randomised controlled trial has just been completed. Neither treatment is available commercially at the time of writing but hypertonic saline is available through public hospital outpatient clinics, and mannitol should be available as a metered-dose inhaler over the next few years.

Is pulmonary rehabilitation of benefit?

All patients with chronic lung disease and dyspnoea warrant some form of pulmonary rehabilitation to prevent the inevitable deconditioning that occurs and exacerbates the dyspnoea. There has not been much research for patients with bronchiectasis, but one study has clearly demonstrated benefit.[6]

What long-term sequelae should I be aware of?

The important long-term sequelae in bronchiectasis are respiratory failure, cor pulmonale, nocturnal hypoventilation, poor nutrition, osteoporosis and haemoptysis.

Respiratory failure can be hypoxic or hypercapnic or both. Hypoxic patients benefit from home oxygen and this can be prescribed by a respiratory physician. Hypercapnic patients may benefit from treatment with non-invasive ventilation, that is bi-level positive airway pressure or variable positive airway pressure.

Cor pulmonale will present with the development of right heart failure symptoms (ankle swelling, often the first thing noticed by the patient) and this should prompt investigation with echocardiography to measure right heart parameters as well as consideration of fluid restriction and diuretics.

Patients with nocturnal hypoventilation will complain of poor sleep, morning headaches and excessive daytime sleepiness. They should be referred to a respiratory/sleep physician for an assessment.

Nutritional deficiency is common in this condition due to the chronic inflammatory state, breathlessness and poor appetite. Patients who are struggling should be weighed each appointment and encouraged to try calorific supplements and see a dietitian.

Osteoporosis is common because patients may have received a lot of prednisone in the past and have nutritional deficiency. Also, a high proportion of patients are postmenopausal women. Broken ribs and vertebral crush fractures can be a problem in patients with lung disease who have become unable to complete physiotherapy and suffer worsening respiratory failure using adequate analgesia. It is best to prevent this with calcium supplementation and bisphosphonates. These patients should probably have an annual bone mineral density scan.

Haemoptysis is dangerous and can occur at any stage of the disease. It requires prompt assessment in a hospital environment. These patients can bleed profusely due to abnormal vasculature, and asphyxiation can develop quickly because of poor gas exchange.

Depending on your local resources, the development of any of these conditions should prompt referral to a specialist centre with multidisciplinary experience in the management of chronic lung disease.

Vaccinations

Patients with bronchiectasis should be considered 'at risk' for serious sequelae from pneumococccal and influenzal illness. They should be given the pneumococcal vaccine and an annual influenza vaccine.

Conclusion

Patients with bronchiectasis experience a lot of morbidity. The management requires attention to a diverse range of concerns, but each intervention is simple and generally easily available. A holistic management strategy will improve health outcomes and quality of life.

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Conflict of interest: none declared

Patient support organisation

The Australian Lung Foundation

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Website www.lungnet.com.au

New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may be limited published data and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Alglucosidase alfa

Myozyme (Genzyme)

vials containing 50 mg powder for reconstitution

Approved indication: Pompe disease

Australian Medicines Handbook Appendix A

Pompe disease is a rare inherited glycogen storage disease caused by a deficiency in the enzyme acid alglucosidase alfa, which breaks down glycogen to glucose. In patients who lack this enzyme, glycogen builds up in various tissues, particularly cardiac and skeletal muscle, leading to cardiomyopathy, progressive muscle weakness and impaired respiratory function. Early-onset disease typically leads to death from cardiorespiratory failure within the first year of life.

This recombinant form of human alglucosidase alfa is produced in Chinese hamster ovary cells. The recommended dose is 20 mg/kg given as an intravenous infusion every two weeks. Its elimination half-life is 2–3 hours.

The efficacy of recombinant alglucosidase alfa (20 mg/kg or 40 mg/kg fortnightly) has been assessed in 18 infants with Pompe disease (aged 7 months or younger) and compared to a historical cohort of 61 untreated infants. All patients given alglucosidase alfa survived until 18 months of age compared with only one of the 61 untreated controls. However, three of the treated infants required invasive ventilatory support during the study. Thirteen of the 18 treated infants had improved motor development by week 52 of treatment with seven of them being able to walk independently. In general, the higher alglucosidase alfa dose (40 mg/kg) did not seem to offer any clear advantage over the lower dose (20 mg/kg).[1]

In a similarly designed trial, 21 infants aged 3–36 months were given alglucosidase alfa 20 mg/kg fortnightly. Of the 16 infants who did not need invasive ventilatory support at enrolment, four had died, two required invasive ventilatory support and ten did not after a year of treatment. Of the five infants who needed ventilatory support at baseline, one had died and four still required ventilation. A historical comparison of the treated infants with 86 untreated infants showed no significant difference in mortality rate. The trial was inconclusive probably due to the heterogeneous study population.

Around half of the children treated with alglucosidase alfa had an infusion-related reaction, which included fever, rash, urticaria, cough, decreased oxygen saturation, vomiting, flushing and tachycardia. These were usually managed by slowing or interrupting the infusion or giving an antipyretic, antihistamine or corticosteriod. Life-threatening anaphylactic reactions have been reported. Pneumonia, respiratory failure or distress, intravenous catheter-related infection, respiratory syncytial virus infection and gastroenteritis have also occurred following treatment.[1]

There is an increased risk of cardiac arrhythmia and sudden death during general anaesthesia for central venous catheter replacement. This has been observed in patients with cardiac hypertrophy. Acute respiratory failure has also occurred in one